

a blinded analysis. The images were analyzed by image analysis software. The density and area of the pixels was proportionate to the amount of the clot formed on the graft surface. **Results:** The pressure gradient between the groups was identical throughout the study, meaning similar flow characteristics were maintained in all branches. The pretreated grafts had fewer blood clots adhered to the surface by direct visual inspection. The image analysis showed 5 vs.39 clots, 0.01% vs. 1.8% clotted area and 62 vs. 5630 clot pixel area between the treated and non-treated grafts respectively, $p < 0.05$.

Conclusion: Pretreatment of the synthetic graft with heparin prior to implantation reduces the risk of early clot formation. This simple practice might be helpful to prevent initial thrombosis of the graft and later occlusion especially in critical situations where the patency of the graft is crucial.

TECHNOLOGY

Drug Coated Balloons

CRT-123

A Novel Nano Particle Sirolimus Delivery Via Coated Balloon

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Objectives: Objective of this study was to develop non-polymeric sirolimus nanoparticle coated balloon and demonstrate in-tissue transfer through DCB in rabbit model.

Background: Drug coated balloon (DCB) is an emerging technology. To date paclitaxel is a choice in DCB. Due to lipophilic properties of sirolimus, short time delivery through DCB is a major challenge. To overcome current limitations, we hypothesized; nanoparticle sirolimus coated on the balloon can provide better delivery and retention.

Methods: We prepared phospholipid encapsulated sirolimus and coated on the balloon with novel coating formulation. The characteristics of the nanoparticle sirolimus DCB was tested in both an in-vitro and preclinical in-vivo models. New Zealand rabbits underwent drug coated balloon dilatation in iliac arteries for pharmacokinetics, confocal microscopy and scanning electronic microscopy studies.

Results: Sirolimus nanoparticles were ~400nm with stable solution. Coating surface was smooth without defect and irregularities. In-tissue uptake of sirolimus was at 1, 7 and 14 days with concentration of 140.6, 15.5 and 5.5 ng/mg, respectively. Sirolimus coated balloon with 3x inflations was also safe in the rabbit iliac arteries. Confocal microscopy showed homogeneous fluorescent tagged nano sirolimus (DTF-nSRL) distribution into the artery wall with intima to adventitia flow. None of the in-vivo investigation has reflected emboli in downward stream.

Conclusion: Present set of experiments showed adequate amount of sirolimus was delivered through non-polymeric DCB. Multiple inflation demonstrated safety to co-relate with actual clinical outcome. Confocal imaging has showed homogenous distribution in cross section and longitude parts. Path of drug travel was to the deepened area of arterial wall upon time from intima to adventitia (Table 1).

Table 1. Depth of DTF-nSRL signal punctuation in rabbit iliac arteries

Time Point	24 hour	3 day	7 day
Depth of penetration	10-20 μ m	10-30 μ m	10-40 μ m

Drug Eluting Stents

CRT-124

Comparative In Vitro Effects Of Paclitaxel, Everolimus, And Tacrolimus On Macrophage-derived Foam Cells, Smooth Muscle Cells, And Endothelial Cells

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Background: Macrophage-derived foam cells (FC) play a key role in atherosclerotic lesion progression. Effects of different drugs used in drug-eluting stents (DES) on FC behavior have not been well characterized. We used an in vitro model to compare effects of paclitaxel, everolimus, and tacrolimus on FC, human coronary endothelial cell (HCAEC), and human coronary smooth muscle cell (HCASMC) viability, FC gene expression, and FC inflammatory cytokine levels.

Methods: FC were derived from human THP1 macrophages with acetylated LDL, followed by treatment with paclitaxel, everolimus, or tacrolimus (10⁻⁵-10⁻¹¹M) for 24 hrs (n=4). HCAEC and HCASMC were similarly treated with all three drugs. Cell lysates and media supernatants were analyzed for apoptosis/necrosis using a Cell Death Detection ELISAPLUS (Roche, Pleasanton, CA) assay. FC lysates were also evaluated for apoptosis (survivin, clusterin) and autophagy (MAP1LC3) gene expression via a Quantigene® Plex assay (Affymetrix, Santa Clara, CA). FC supernatants were analyzed for MCP1 levels via a Procarta® immunoassay (Affymetrix). Statistical significance was set at $p < 0.05$ by ANOVA/Holm's t-test.

Results: FC apoptosis was significantly increased compared to control at 10⁻⁵M for both everolimus and paclitaxel, with no effects on FC necrosis for both drugs. Tacrolimus did not affect FC apoptosis or necrosis. Paclitaxel (10⁻⁵M) significantly increased clusterin and decreased survivin expression in FC. Tacrolimus did not affect gene expression while everolimus (10⁻⁵M) significantly increased MAP1LC3 and clusterin ($p=0.10$) and decreased survivin expression in FC. Everolimus (10⁻⁵M) significantly decreased MCP1 in FC supernatants. Effects of all three drugs on HCASMC and HCAEC viability were also explored. While everolimus and tacrolimus did not affect apoptosis or necrosis, paclitaxel (10⁻⁵M) significantly increased HCASMC and HCAEC apoptosis and necrosis.

Conclusion: The three drugs explored in this study have variable effects on FC, HCASMC, and HCAEC. Unlike paclitaxel and tacrolimus, everolimus may inhibit FC accumulation in atheromas through selective autophagy/apoptosis of FC and inhibition of monocyte recruitment into the arterial wall.

CRT-125

Do Second-Generation Drug-Eluting Stents Outperform First-Generation Drug-Eluting Stents When Used in "Full Metal Jacket" Percutaneous Coronary Intervention Procedures?

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Background: Diffuse coronary lesions are often treated with long and overlapping drug-eluting stents (DES) creating a full metal jacket, however the impact on clinical outcomes comparing different generation DES has not been described.

Methods: We conducted a retrospective analysis of 98 patients with full metal jacket stenting, defined as the total and continuous stent length of ≥ 50 mm in a single vessel, treated using either first-generation (sirolimus- and paclitaxel-eluting) DES or second-generation (everolimus-eluting) DES.

Results: Full metal jacket stenting was performed in 36 patients/71 lesions with second-generation DES (Xience V or Promus); and 62 patients/151 lesions with first-generation DES (Cypher or Taxus). Baseline characteristics were similar between the groups. More second-generation DES were used per patient than first-generation DES (3.2 vs. 2.6, $p < 0.001$); mean stent length (23.9 vs. 25.3mm) and diameter (2.9mm in both) were similar ($p=NS$). Angiographic success was 100% in both groups. At 1-year

follow-up, a reduction in major adverse cardiac events (MACE) was observed with second-generation compared to first-generation DES (5.6 vs. 16.1%, $p=0.20$), driven by a four-fold decrease in target vessel revascularization (2.9 vs. 14.8%, $p=0.09$), although not reaching statistical significance. Only 1 patient (1.6%) in the first-generation DES and none in the second-generation DES had definite stent thrombosis (Table).

Conclusion: In this study of full metal jacket stenting for diffuse lesions, second-generation DES compared to first-generation DES demonstrated a favorable trend toward reduction in repeat revascularization and MACE at 1-year with acceptable safety profile.

Clinical outcomes at 1-year between first and second generation DES

	Second-generation DES (n=36)	First-generation DES (n=62)	P value
Major adverse cardiac events	2 (5.6%)	10 (16.1%)	0.20
Death	1 (2.8%)	1 (1.6%)	1.00
Q-wave myocardial infarction	0	0	-
Target vessel revascularization	1 (2.9%)	9 (14.8%)	0.09
Target lesion revascularization	1 (2.9%)	7 (11.5%)	0.25
Definite stent thrombosis	0	1 (1.6%)	1.00

Emerging Devices & Innovative Therapies

CRT-126

Three Years Follow Up Data Demonstrate Safe And Effective Treatment Of De Novo Calcified Coronary Lesions By Orbital Atherectomy System

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Background: Coronary Artery Disease continues to be a widespread and growing problem worldwide. Performing PCI on calcified lesions can lead to higher MACE rates and stent under expansion/malapposition. The Orbit I trial was conducted to evaluate the safety and performance of the Diamondback 360 Orbital Atherectomy System (OAS) (Cardiovascular Systems, Inc., St. Paul, MN, USA) for the treatment of calcified coronary lesions.

Methods: From May 2008 to July 2008, 33 patients were enrolled in ORBIT I study based on several criteria, including a de novo, coronary lesion with stenosis $\geq 50\%$ and $\leq 100\%$ and at least one quadrant of calcification via IVUS. The patients were treated with OAS prior to stent placement. The patients were followed for 36 months at Care Institute of Medical Sciences, Ahmedabad, India to evaluate the MACE rate.

Results: Of the 33 patients, 90.90% ($n=30/33$) were males with an average age of 54.9 years. The ACC/AHA lesion class was: Type A 6.06% ($n=2/33$); Type B1 33.33% ($n=11/33$); Type B2 60.60% ($n=20/33$). The % diameter stenosis was 85.75%; lesion length was 15.90 mm. The procedural success was 97% (32/33) with one case where IVUS/device was not able to cross the lesion due to severe calcification. All stents were successfully deployed with $0.3\% \pm 1.8\%$ residual stenosis. The observed MACE rate was as follows: in-hospital 6.06% ($n=2/33$); 30 days 9.09% ($n=3/33$); 6 months 12.12% ($n=4/33$); 24 months 15.15% ($n=5/33$); and 36 months 18.18% ($n=6/33$). MACE rate comprised of 2 patients with a non Q-wave MI in-hospital; one patient with non Q-wave MI at 30 days that led to TLR; and one patient with cardiac death at 6 months, 24 months and 36 months, respectively.

Conclusion: This case series demonstrates that OAS safely and effectively modified calcified lesions and facilitated stent delivery in this difficult-to-treat plaque morphology, which continues up to three years post index procedure.

CRT-127

Hyperinvasive Approach To Out-of Hospital Cardiac Arrest Using Mechanical Chest Compression Device, Prehospital Intraarrest Cooling, Extracorporeal Life Support And Early Invasive Assessment Compared To Standard Of Care. A Randomized Parallel Groups Comparative Study. "Prague Ohca Study". Results Of Presimulation And Simulation Phase

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Background: Out of hospital cardiac arrest (OHCA) has a poor outcome. Recent non-randomized studies of ECLS (extracorporeal life support) in OHCA suggested further studies to define population that would benefit from ECLS. Ongoing prospective randomized study compares prehospital intraarrest hypothermia combined with mechanical chest compressions, intrahospital ECLS and early invasive assessment in refractory OHCA of presumed cardiac origin compared to a standard of care. This abstract describes methodology of the trial and results of presimulation and simulation phase.

Methods: Patients with witnessed OHCA without ROSC (return of spontaneous circulation) after a minimum of 5 minutes of ACLS (advanced cardiac life support) by emergency medical service (EMS) team are randomized to standard vs. hyperinvasive arm. In hyperinvasive arm, mechanical compression device together with intranasal evaporative cooling is instituted and patients are transferred directly to cardiac center under ongoing cardiopulmonary resuscitation. After admission, ECLS inclusion/exclusion criteria are evaluated and if achieved, veno-arterial ECLS is started. Invasive investigation and standard postresuscitation care follows immediately. Patients in standard arm are managed on scene. When ROSC is achieved, patients are transferred to cardiac center and further treated as per recent guidelines. During the presimulation phase mechanical chest compression device has been used routinely in all patients with OHCA, during the simulation phase patients were to practice the logistics of the study.

Results: Since January until October 2012 we enrolled 40 patients, 32 to presimulation and 8 to simulation protocol. Average age was 61 years (21-87), 85% were men. Acute coronary syndrome was the cause in 21 (53%) patients, STEMI 17 (43%), cardiac origin of OHCA was identified in 63% of patients. Average time until ROSC was 40 minutes, median 32 minutes (15-120). Twenty (50%) patients survived, CPC (Cerebral Performance Category) 1+2 during hospitalization reached 15 of 20 survivors (75%) and 1 of 20 nonsurvivors (5%). Survival in patients admitted under ongoing CPR was 5 of 17 (30%).

Discussion: A combined, hyperinvasive approach to refractory OHCA is a viable option with challenging preliminary results. The protocol is opened for sharing by other cardiac centers with available ECLS and cathlab teams trained to admit patients with refractory cardiac arrest under ongoing CPR. Supported by IGA NT 13225-4/2012, registered under ClinicalTrials.gov NCT01511666.

Other

CRT-128

Renal Artery Denervation in Chronic Kidney Disease Patients

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Renal Denervation Therapy (RDN) have been proven to be useful in resistant hypertension patients. The Symplicity Trials did not include patients with renal disease whereas, a significant number of end stage renal disease (ESRD) patients who have resistant hypertension despite being on multiple drugs and the benefits of RDN in such patients have not been reported.